A Dissertation on

THE OCCURRENCE OF OBSTRUCTIVE SLEEP APNEA AND ITS

COMPLICATIONS IN OBESE INDIVIDUALS

Dissertation submitted to

THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY

CHENNAI-600 032

With partial fulfillment of the regulations

For the award of the degree of

M. D. GENERAL MEDICINE

BRANCH I

INSTITUTE OF INTERNAL MEDICINE

MADRAS MEDICAL COLLEGE,

CHENNAI - 600003.

MARCH 2009

CERTIFICATE

This is to certify that this dissertation entitled " **A STUDY ON THE OCCURRENCE OF OBSTRUCTIVE SLEEP APNEA AND ITS COMPLICATIONS IN OBESE INDIVIDUALS**" submitted by **Dr. VENKATESH RAJKUMAR.S** , Post graduate student of General Medicine, Institute of Internal Medicine, Madras Medical College, Chennai – 600003 is a bonafide record of work done by him during the academic years 2006 – 2009.

Prof. A.R. MALATHY, M.D.,
Additional Professor of medicine,
Institute of Internal Medicine,
Madras Medical College &
Government General Hospital,
Chennai - 600003.

DIRECTOR,
Institute of Internal Medicine,
Madras Medical College &
Government General Hospital,
Chennai – 600 003.

THE DEAN,
Madras Medical College& Government General Hospital,
Chennai – 600003.

DECLARATION

I solemnly declare that this dissertation titled "A **STUDY ON THE OCCURRENCE OF OBSTRUCTIVE SLEEP APNEA SYNDROME AND ITS COMPLICATIONS IN OBESE INDIVIDUALS" is** done by me at Madras Medical College & Govt. General Hospital, Chennai during the academic years 2006-2009 under the guidance and supervision of **Prof. A.R.Malathy, M.D.** This dissertation is submitted to the Tamil Nadu Dr. M.G.R. Medical University towards the partial fulfillment of requirements for the award of M.D. Degree in General Medicine (Branch – I).

Place: Chennai Dr. VENKATESH RAJKUMAR.S

Date:

SPECIAL ACKNOWLEDGEMENT

I gratefully acknowledge and sincerely thank **Prof. T.P. Kalaniti, M.D.,** Dean, Madras Medical College and Government General Hospital Chennai, for granting me permission to utilize the resources of the Institution for my study

ACKNOWLEDGEMENTS

I would like to express my sincere gratitude to my beloved professor and Director, Institute of Internal Medicine **Prof. C.RAJENDIRAN, MD,** for his guidance and encouragement.

This is one another fine moment to express my gratitude and indebtedness to my beloved chief, **Prof.A.R.Malathy, MD,** for her motivation, advice and valuable criticism, which enabled me to complete this work.

I am extremely thankful to my former unit chief **Prof. V.K. Rajamani ,MD,** Retired Additional Professor , Institute of Internal Medicine, for his constant guidance and encouragement in the initial periods of this study.

I am extremely thankful to **Prof. M. Jubilee, MD,** Additional Professor of Medicine, Institute of Internal Medicine for her constant and untiring help and guidance.

I am thankful to **Prof. Mythily Baskaran MD,** formerly Head of the department, Department of Physiology, for granting permission to do polysomnography in Physiology sleep Laboratory.

I am also grateful to other assistant professors who helped me complete the study.

I am extremely thankful to Assistant Professors of my parent unit, **Dr.G.Rajan,MD,** and **Dr.S.Gopalakrishnan MD,** for their co-operation and guidance.

I am thankful to all my Postgraduate colleagues for their constant support and sharp constructive criticism.

I should thank each and every patient for the whole hearted co-operation despite the morbidity they suffered.

I should thank each and every member of my family for the constant support and encouragement.

TABLE OF CONTENTS

Introduction

Obstructive sleep Apnea/Hypopnea syndrome (OSAHS) is one of the most important medical conditions identified in the last fifty years. It is a major cause of morbidity, a significant cause of mortality throughout the world, and the most common medical cause of daytime sleepiness. Central sleep apnea is a less common clinical problem.

As the various ill effects of obesity are becoming increasingly recognized, so does the prevalence and the adverse health effects of OSAHS. It is now proven beyond doubt that OSAHS plays a significant role in Hypertension, Diabetes Mellitus, coronary artery disease, cognitive decline etc.

But even now in our part of the world, it is a less well recognized and less commonly made diagnosis and it is largely overlooked.

This study is done to see if it is really a commonly occurring problem in obese individuals and what are the complications associated with it.

AIMS AND OBJECTIVES

1. To study the occurrence of Obstructive sleep apnea –hypopnea syndrome in obese individuals

2. To study the various complications associated with obstructive sleep apnea – hypopnea syndrome and to find their prevalence.

Review of literature

Sleep disorders of breathing includes Obstructive sleep Apnea/ Hypopnea syndrome (OSAHS) and upper airway resistance syndrome (UARS). Obesity and craniofacial dysmorphism are the major risk factors for these syndromes.

Epidemiology: OSAHS was first recognized during polysomnographic monitoring of severely obese patients with the pickwickian syndrome (1).

Epidemiological studies based on general population or community based cohorts between 30 and 60 years of age estimate that 2-5% of population is affected by OSAHS (2-8). It should be noted that these figures mainly applies to whites. The incidence may vary in other ethnic groups. The prevalence is twice common in women as in men. The syndrome also occurs in childhood usually associated with tonsillar or adenoid enlargement and in the elderly the frequency is slightly lower. Irregular breathing during sleep without daytime sleepiness is much more common, occurring perhaps in one fourth of middle aged males. However as the individuals are asymptomatic, they do not have OSAHS and there is no evidence as of now that these events are harmful.

1. HISTORICAL PERSPECTIVES

1.1 BEGINNING OF THE ERA OF SLEEP MEDICINE:

Modern scientific research on sleep patterns and sleep mechanisms began in the nineteenth century with the development of electrophysiological tools, needed to study small amplitude biopotentials. In 1875 Caton recorded spontaneous electrical activity from brains of animals. Brain biopotentials in humans were recorded in 1929, by Berger from exposed cortex from patients from whom a piece of skull had been removed. He coined the term electroencephalography to describe these small biopotentials. Berger reported that the EEG activity was faint when subjects were alert and strong when they were relaxed. In 1937 Loomis et al reported all- night EEG studies in humans and confirmed Berger's findings. In 1953 Aserinsky and Kleiman identified the unique sleep stage, where low voltage fast EEG activity occurred with bursts of eye movements. Dement and Kleiman recognized it as a state associated with dreaming and coined the term "REM (Rapid eye movement) sleep".

The importance of sleep in the pathogenesis and treatment of medical illness have been observed from time to time by astute physicians. Beyond these observations, discoveries of sleep related changes in basic physiology and their possible role in the pathogenesis of disease awaited the era of modern electrophysiology. The discovery of REM sleep in the 1950s along with the automatic alterations associated with this state showed that important physiological changes are associated with sleep. The decade of 1960s witnessed very little interest in medical as opposed to psychiatric application of sleep research. With the discovery of sleep related breathing disorders in the 1960s, the attention was then focused to variety of different sleep related breathing disorders in children and adults.

1.2HISTORICAL ASPECTS OF OBSTRUCTIVE SLEEP APNEA SYNDROME

The syndrome of obstructive sleep apnea provides a unique example of those disorders where a syndromic description of the disease existed long before its scientific documentation. First described by Charles Dickens in the posthumous papers of the Pickwickian club, in 1837, a boy named Joe. Joe was described as an extremely fat, persistently hypersomnolent character. The term “Pickwickian

syndrome" derives from this. In 1889 observations were made by the British physician Caton and French man Lameq that certain people with excessive daytime somnolence tend to have periods of suffocation during sleep. The term 'Pickwickian' was first coined by Sir William Osler in 1918, to describe obese, hypersomnolent patients. Observations were made in 1939 by Kerr and Langer that such patients develop cardio respiratory problems, like Cor pulmonale and cadiac failure. The principal clinical features of the Pickwickian syndrome were reviewed by Burwell et al in 1956, Belner in 1954 and 1962. Alexander and colleagues described a 'Joe' type of Pickwickian characterised by Obesity and hypersomnolence alone. Repeated attacks of obstructive sleep apnea were noted to occur in these Pickwickian by Gastaut and colleagues in 1964-65. The first case report of a patient with presumed Obstructive sleep Apnea was presented by jung and Kalls in 1965, remarking that the patient had sleep apnea for 10 years prior to the development of the Pickwickian syndrome. The first cinematographic study of obstructive sleep apnea was done by Schwartre and Scanele in 1967, when the oropharyngeal collapse during apneic episodes was demonstrated. The first international meeting on 'Hypersomnolence and periodic breathing' was organised in 1972 by Lugaressi and Sadenil. In the decade that followed clinicians started applying their knowledge of sleep physiology to the sleep apnea syndrome and tracing the various components underlying the syndrome (9).

By the early 1980s a methodology to study sleep had been described in detail. The description of these sleep related phenomenon accomplished two goals in identifying sleep as a legitimate area of medicine and science:

1. Sleep was objectively described by measurable physiologic changes.
2. Unique physiological changes specific to sleep were identified.

2. PHYSIOLOGICAL ASPECTS OF SLEEP

2.1CLASSIFICATION OF SLEEP WAKEFULNESS STAGES

The most widely accepted classification system in use today is that of Rechscaffen and Kales. An important premise of this scoring system is that REM sleep, NREM sleep and wakefulness are fundamentally different stages of consciousness, as determined by both electrographic and physiologic variations.

The essential electrographic parameters used in the determination of sleep stages are the electroencephalogram (EEG), electrooculogram (EOG) and electromyogram (EMG). Briefly the Rechschaffen and Kales guidelines for

assigning sleep stage classification to each 20-60 seconds scoring epoch is as follows:

Waking: The EEG activity during alert wakefulness predominantly consists of low amplitude, high frequency (13-35 Hz) beta activity, accompanied by high EMG activity and frequent eye movements. With relaxation a sinusoidal alpha activity (8-13Hz) is superimposed on the β pattern. As the subject changes from relaxed, alert condition to drowsiness, the EEG activity slows to a frequency nearer the end of alpha range.

STAGE 1 NREM SLEEP: This is a transitional stage between waking and sleep that typically lasts 1-7 minutes. The EEG shows low amplitude, mixed frequency activity in the beta and theta (4-7Hz) range. Later slower frequencies begin to predominate and high amplitude (up to 200 μv) vertex sharp waves may appear. EMG activity is usually higher than other sleep stages. EOG often shows disconjugate slow rolling eye movements lasting 1 second or more.

STAGE 2 NREM SLEEP: This stage is recognized by the presence of sleep spindles and 'K' complexes. Sleep spindles are sinusoidal rhythm (12-20Hz) of brief duration. The K- complex is a high amplitude negative sharp wave followed immediately by a slower positive component.

STAGE 3 NREM SLEEP: This stage is recognized by the presence of high amplitude slow wave (greater than 75μv) peak to peak, 2Hz or slower, appearing in 20-50% of the scoring Epoch. EMG activity is usually low and eye movements are absent.

STAGE 4 NREM: This stage is defined by the presence of slow waves in more than 50% of the Epoch. Stage 3 and 4 are often combined.

NREM is a physiologically quiet and stable stage. Heart rate and respiration tend to be slower and regular and muscles relaxed.

REM SLEEP: The EEG during REM sleep consists of mixed frequency, low voltage activity closely resembling the EEG of stage 1 NREM. REM sleep is characterized by a broad spectrum of physiological changes. EMG activity is lowest and rapid conjugate eye movements occur throughout the REM periods.

'Phasic' episodes within the REM sleep are characterized by high degree of autonomic variability, including elevated and irregular heart rate, respiratory rate and blood pressure. During 'Tonic' REM sleep these variables are more constant (10).

2.2 PHYSIOLOGIC VARIATIONS OF CARDIORESPIRATORY PARAMETERS DURING SLEEP.

2.2.1 SLEEP AND BLOOD PRESSURE

Early studies employing indirect methods to record Blood pressure (BP) documented consistent but variable reduction in systemic blood pressure during sleep. Synder et al first correlated EEG with respiration, heart rate and systolic BP measured at 5 minutes intervals with a sphygmomanometer in 12 healthy subjects during 2-3 nights of uninterrupted sleep (11). They described a fall in blood pressure averaging 20% to a minimum about 2 hours after the beginning of sleep, with gradual rise by rest of the night to a level comparable to that at sleep onset. Richardson et al also correlated the EEG with Blood pressure and heart rate and noted that waking even for brief periods always resulted in elevation of BP and Heart rate(HR) which coincided with the occurrence of the α rhythm and averaged 13/11 mmhg and 5 beats/minute respectively (12). Smyth et al further demonstrated that there is no nocturnal rhythm of BP independent of sleep (13). As early as 1912, Brookes and Carroll noted that frequent interruptions in sleep prevented the fall in BP (14). Litter et al measured continuous intra arterial BP in 27 unrestricted volunteers and demonstrated that irrespective of the use of antihypertensive drugs, the blood pressure falls during sleep and rises on awakening and continues to rise with physical activity. The mean arterial pressure

was found to decrease by an average of 5-9% during NREM sleep stages 3 &4, when compared to awake resting stage. During REM sleep, BP fluctuated considerably and averaged values about 5% greater than immediately preceding or succeeding values during NREM(15).With the availability of ambulatory blood pressure monitoring devices, the data on the blood pressure variability throughout the day and night became available. During such measurements the blood pressure is found to dip by 5-10% towards the later part of the night (16).

2.2.2 SLEEP AND HEART RATE:

Heart rate normally decreases by 5-8% during NREM sleep. During REM sleep heart rate is variable with the mean rate approximating the resting awake values (17).

CARDIAC ARRYTHMIAS DURING SLEEP

The prevalence of cardiac arrhythmias has been evaluated in young, middle aged and elderly normal subjects using Holter monitoring. The results have indicated that ventricular ectopic activity is frequently observed in normal

population; its prevalence increases with age. Most of the studies show a decrease in the frequency of ventricular ectopy during sleep (18, 19, 20, and 21)

Sinus arrhythmia was found to be the most frequent nocturnal dysrrhythmia occurring in 50% of young men. About 30% had sinus pauses of 1.8-2.6 seconds duration and 6% had episodes of first degree block (18). The prevalence of bradyarrythmias tend to decrease with age and is lower in females (19, 20,22).

3. OBESITY AND SLEEP APNEA

3.1 EPIDEMIOLOGIC DATA:

In his review of sleep apnea syndromes Guilleminault found that 20% of the subjects had normal weight, another 20% were 15% or less overweight, 30% were 16-30% overweight and 40% were 31-400% overweight. Thus approximately 70% of the patients were found to be obese (23). Boudoulas studied 120 consecutive patients referred with excessive daytime sleepiness and concluded that patients with sleep apnea were usually obese (24). In another study the prevalence of OSA in obese middle aged men, who had been selected for weight reduction surgery was found to be 38%, most of whom were symptomatic (25).

3.2 MECHANISMS: UPPER AIRWAY STRUCTURE

Obstructive sleep apnea occurs because of recurrent occlusion of the upper airway during sleep. Upper airway imaging techniques (eg. CT scanning of the pharynx), have provided important insights into the pathogenesis of OSA (26). Lateral cephalomerty has evolved as a simple and well standardized imaging technique consisting of radiograph of head and neck with specific emphasis on bony and soft tissue structures (27). Cephalometry has demonstrated a variety of abnormalities of craniofacial and upper airway soft tissue anatomy that may predispose patients to upper airway obstruction during sleep and that are also related to severity of OSA. Patients with OSA have been shown to have, small posteriorly placed mandible, a narrow airway space, an enlarged tongue and soft palate, and an inferiorly placed hyoid bone. Posterior hyoid space, hyoid position and soft palate and tongue size have all been shown to be significant determinants of apnea severity (18, 28, 29, 30). It remains unclear whether craniofacial abnormalities or soft tissue changes are the most important determinants of OSA in most patients.

Obesity occurs in most patients with OSA and is considered to be a major risk factor for its development. Neck circumference (NC) is a simple clinical measurement that reflects obesity in the region of the upper airway. Patients with OSA have been shown to have thick necks when compared with both non-apneic

snorers and weight matched controls (29, 31). Furthermore NC correlates with several soft tissue variables, measured from lateral cephalometry, and correlates better than body mass index with apnea severity (31). This suggests that obesity mediates its effect in OSA through fat deposition in the neck. However not all patients with OSA are obese, Ferguson et al found that in comparison to obese , patients with OSA , who have increased upper airway soft tissue, non obese OSA patients have abnormal craniofacial structure, as detected by lateral cephalometry (32).

3.3 DISTRIBUTION OF BODY FAT AND GENDER DIFFERENCES

Studies have shown a difference in the prevalence of OSA in men and women of equivalent BMI. Rajala et al studied 13 men and 14 women of BMI approximately 40kg/m^2 and found the occurrence of OSA to be 76.9% in men and 7.1% in women (33). This suggests that the differences in fat distribution in men and women contribute to the differences in the development of OSA. Millman et al found a greater degree of upper body obesity, as reflected by higher waist to hip ratio, subscapular skin fold and neck circumferences and smaller hip circumferences in men. The men also had more severe degree of OSA compared to women (34).

Differences in body fat distribution may not be the only factor causing gender differences in the occurrence of OSA. Schewas et al using cine computed tomography found that in men the change in pharyngeal area is larger with changing lung volume, implying a greater tendency for the airway to collapse (32).

An alternate explanation is in the gender related differences in the ventilatory control that predisposes obese men rather than obese women to develop OSA (35, 36).

3.4 WEIGHT REDUCTION AND OSA

Further information in the role of obesity in the sleep apnea has been gained by doing sleep studies on obese patients with obstructive apnea before and after weight loss. Methods reported for weight loss among patients with obstructive sleep apnea have included ileal bypass, gastric partitioning or gastroplasty and starvation. These reports in general have shown a marked improvement in patients symptomatically, especially decreased somnolence, a decrease in the number of apnea episodes and improvement in oxygenation of the patient (37, 38). Block felt the improvement in four morbidly obese patients who had lost an average of 108 kg was so marked that it proved obesity was a cause than an effect of the sleep apnea syndrome (38).

Orr et al reported that patients who were hypersomnolent and had obstructive sleep apnea weighed more, had lower waking arterial O2, during sleep, than did the asymptomatic patients with a comparative degree of obstructive sleep apnea (39). Losing weight often corrects hypoxemia in obese patients. Apart from apnea, hypoxemia in obese patients occurs because of the alveolar hypoventilation related to elevated diaphragm and further mismatch of ventilation and perfusion in supine position.

Not all studies have found weight reduction helpful in the treatment of obstructive sleep apnea. The weight loss was noted to be partial and temporary in one review. In a second series it was found to have no effect on clinical symptoms or respiration. The amount of weight loss might not have been sufficient (40).

3.5 ROLE OF ENDORPHINS AND ENCEPHALINS: Another new area of research to link obesity, sleep apnea and alveolar hypoventilation are the endorphins and encephalins. Marguls et al found elevated concentration of β-endorphins in the pituitaries of obese mice (41). The endogenous opioids have been considered to control the initiation of feeding drive especially during stress inducing stimulus. McCloy and McCloy postulated that obesity was simply an auto

addiction to the endogenous opioid peptides. O'Brien found a relationship between endorphin activity and human obesity (42).

Endorphins have been related to changes in ventilatory drive, causing bradypnea, apnea and hypo-ventilation. B-endorphin injected intracisternally in lightly anaesthetized dogs resulted in marked respiratory depression and diminished ventilatory response to carbon dioxide in one study (43). The elevated β-endorphin levels found in the brains of obese people may play a role in lowering the threshold for development of hypoventilation during sleep. These postulates need further investigation.

4. SLEEP APNEA AND HYPERTENSION

Sleep apnea and systemic hypertension are common health problems affecting the middle aged and older population. Though common in males the prevalence of both hypertension and sleep apnea in post menopausal women nearly equals that of men of same age. Many recent reports noted increased risk of systemic hypertension in sleep apnea syndromes. It has been suggested that apnea lead to sustained daytime elevation of blood pressure and ultimately hypertension.

4.1 THE APNEA HYPERTENSION CORRELATION

Sleep apnea and hypertension are linked by epidemiological studies. About 50% of all patients with sleep apnea are hypertensives (44, 45). Conversely prevalence of sleep apnea in patients with hypertension approximates about 30 %(46, 47, 48). Despite this association, apnea has not been proved to be a direct causal factor for hypertension. The cause effect relationship is further compounded by factor of age, and presence of obesity both of which affect the incidence of sleep apnea.

In contrary to the normal dip in BP in normal and hypertensive individuals, the BP in patients with sleep apnea may fail to dip. The BP rises slowly throughout the night in such patients. This pattern is also observed in preapneic snorers (49). This causal role of apnea in hypertension in some treated apnea patients (50, 51, 52). In the study by Fletcher et al, 8 males experienced a lowering of BP from 149/95 to 139/90 without antihypertensive medications after treatment of sleep apnea (53). Guilleminault described two children with sleep apnea in whom tracheostomy reduced BP from 150/100 and 160/105 to 120/80 and 125/80 respectively. There have been reports of lowering of BP in patients with sleep apnea treated with nasal CPAP. Wilcox examined systolic BP in 19 subjects treated with nasal CPAP for 8 weeks and found a reduction in BP in both normotensive and hypertensive subjects (54).

4.2 EPIDEMIOLOGIC EVIDENCE OF CASUALTY

The first study to examine apnea as a potential cause of primary hypertension included 16 hypertensive subjects where clinical histories suggested sleep apnea. Eleven were found to have more than 10 apneic events/hr (40). Since this lacked age, weight and sex matched controls, the importance is partially compromised.

Kales et al subsequently performed polysomnography in 50 Hypertensive and 50 normotensive patients matched for age but not weight. Fifteen (30%) of the hypertensive subjects were diagnosed as having sleep apnea with mean index of 22.4events/hr (47). Fletcher et al examined the prevalence of sleep apnea in 46 men with essential hypertension and 34 normotensive men matched for age and weight. Fourteen hypertensive men and 3 controls had sleep apnea defined as more than 10 apnea/hr (53). Williams et al studied 23 hypertensive subjects and 8 age and weight matched normotensive subjects and found that 35% of the hypertensive subjects had sleep apnea. Hypertensive subjects were removed from medications at the time of study and patients with apnea were more obese than patients without apnea (53).

Some other studies have not demonstrated a higher prevalence of apnea in hypertensive population. Hirshkowitz et al found no difference in apnea index between 38 untreated hypertensive and 53 normotensive males (55). Warley et al recorded overnight arterial desaturations at home in 30 men with untreated essential hypertension and compared the data to 30 normotensive controls, matched for age, height and weight (56). These were not full polysomnographic studies and respiration was not monitored.

A study by Hofstein et al supports the association between self reported snoring and systemic hypertension. They studied 1415 patients; Multivariate regression analysis showed age, male sex, AHI and BMI to contribute to variability in BP. It concluded that snoring in absence of apnea does not contribute to hypertension (57).

Hia et al studied ambulatory BP measurements during an entire 24 hr period in 147 patients and compared the pattern in patients with OSA and in non apneic snorers, with the general population. They found an association between hypertension and sleep apnea independent of age, obesity and sex (58). More recently Pankov et al also used 24 hour BP monitoring at 15 minute intervals in 93 subjects and found an association between nondipping and apnea severity (58).

In summary, the epidemiological evidence implicating apnea as a cause of primary hypertension remains controversial some studies have been done without normotensive controls matched for weight making it impossible to sort out the effect of obesity as a contribution for both these diseases. In studies where subjects remained on hypertensive drugs, the possibility remains that the drugs contributed to the disordered breathing during sleep.

4.3 APNEA IN ACUTE BP ELEVATION

4.3.1 ACUTE CHANGES ASSOCIATED WITH APNEA:

Apnea exerts several acute cardiothoracic, neural and hemodynamic effects. They are:

a) Wide fluctuations in intrathoracic pressure to values as low as -90cmH2O

b) Gradual lowering of blood oxygen and rise in blood carbon dioxide level with resultant stimulation of peripheral chemoreceptors

c) Vagal hypertonia associated with hypoxemia and stimulation of baroreceptors resulting in slowing of heart rate

d) Decreased stroke volume (right ventricular overfilling with septal shift)

e) Increased afterload (greater transmural pressure) from the deep negative intrathoracic pressure

f) Surge of sympathetic activity to vascular smooth muscle causing vasoconstriction in certain vascular beds.

With resumption of normal breathing, release of bradycardia, normalization of right ventricular preload and release of left ventricular afterload contributes to sudden increase in cardiac output. When the larger blood volume meets the constricted peripheral vascular bed, an acute post apneic increase in blood pressure occurs (59, 60).

4.3.2 EFFECTS OF ACUTE HYPOXEMIA

The most striking acute pathophysiologic change during sleep apnea in humans is episodic hypoxemia, often to SaO2 levels below 50% and PaO2 levels less than 30mmHg.

In patients with severe apnea, urinary catecholamines are found to be elevated (61). Using microneurography, it was found that acute hypoxia which

elevates blood pressure also elevates postganglionic sympathetic activity(62).Such evidence suggests that diurnal elevation in blood pressure might be mediated by recurrent chemoreceptor activation and increased/ prolonged sympathetic nerve activity.

4.3.3 ACUTE HYPOXEMIA DURING HUMAN APNEA

Indirect evidences indicate hypoxia as the main trigger for acute blood pressure elevation during apnea. Shepherd observed repetitive apneas in 10 subjects while measuring intra-arterial blood pressure. He noted an apparent positive relationship between oxyhemoglobin desaturation and blood pressure elevation with a correlation co-efficient of 0.58 in some individuals (63). Van den Aardweg and Karemaker asked males to simulate apnea by holding their breath voluntarily under hypoxic conditions (allowing desaturation). The blood pressure in these subjects rose to abnormal values (mean> 150/90 mmHg) during hypoxic stimulation but remained stable during hyperoxic ones (64). The finding indicates that hypoxia was a necessary component for an intra-apneic rise in blood pressure.

Lavie et al applied automated 24 hr BP monitoring to 38 patients with Obstructive sleep apnea. They found that Apnea- Hypopnea index, age total sleep-

time and minimal level of apnea desaturation accounted for 52% and 54% of the total variance in diastolic and mean 24 hr blood pressure respectively (65).

Hedner et al documented similar correlation between nadir oxyhemoglobin desaturation in 17 apneic subjects. The same study demonstrated that patients with obstructive sleep apnea, regardless of their resting blood pressure, have an increased pressure response to induced hypoxia compared to non- apneic controls (66).

Some investigators doubt about the role of hypoxia alone as the major inducer of blood pressure elevation in the setting of sleep apnea. In one study, the authors investigated the effect of non specific arousal from sleep on acute blood pressure changes. Bursts of auditory stimuli during sleep acutely elevated systemic blood pressure upto 20% in 5 normal adults (67). Ringer et al also attributed blood pressure elevation following apnea to arousal rather than hypoxia (68).

In summary, although many factors may play roles in the acute blood pressure elevation during apnea, the best investigated one is acute hypoxia.

Some studies show correlation between the level of acute blood pressure elevation and degree of hypoxemia; the authors question hypoxia as a major determinant in acute hemodynamic response to apnea and suggest other mechanisms such as arousal.

4.3.4 APNEA AND CHRONIC BP ELEVATION

A number of factors associated with sleep apnea are thought to play a role in the mechanisms for long term diurnal blood pressure elevation. They are:

a) The direct effect of episodic hypoxia and hypercapnia on chemoreceptors and sympathetic activity.

b) Modification of the cardiovascular system (including fluid balance) in response to marked fluctuation in negative intrathoracic pressure, during obstructed breathing.

c) Generalized stress from disruption of sleep

d) Genetic factors

e) Age

4.3.4 .1 THE ROLE OF CHEMORECEPTORS

Chemoreceptors adapt in a long term fashion to hypoxia and hypercarbia and play a role in determining baseline blood pressure. It has been demonstrated that young subjects with mild hypertension have an increased ventilatory and pressure

responsiveness to isocapneic hypoxia. Augmented resting ventilatory drive dependent on peripheral chemorecptors has been documented in hypertensive subjects, and potentiation of excitatory sympathetic nerve responses to hypoxia has been shown in borderline hypertensive subjects.

It has been hypothesized that long term episodic hypoxia during obstructive sleep apnea resets the chemoreceptor reflex drive to a higher level, causing a chronic increase in sympathetic tone and initiating hypertension (59, 60).

4.3.4.2 THE SYMPATHETIC NERVOUS SYSTEM IN ACUTE APNEA

Using microneurography of perineal muscle nerves during obstructive and non-obstructive apneas in humans, Hedner et al demonstrated that sympathetic nerve activity increased markedly throughout the course of apnea, reaching a peak at the onset of ventilation followed by an abrupt drop (69).

Fletcher et al demonstrated elevated nor epinephrine and not metanephrine in patients with severe apnea, with normalization after tracheostomy (70). Mannone et al demonstrated that both nor epinephrine and epinephrine were elevated at night in subjects with obstructive sleep apnea. Only epinephrine excretion decreased on the subsequent night with elimination of apnea by nasal CPAP (71).

The contribution of hypoxia in causing increased sympathetic nerve activity is demonstrated in a study by Somers et al. using perineal nerve recording in normal humans the authors demonstrated increased activity during induced hypoxia and stimulated apnea (72).

Apnea may enhance sympathetic activity via the Bainbridge reflex, as a result of increased right atrial filling. (Muller's maneuveur) and hypoxic pulmonary vasoconstriction (73).

4.3.4.4 CHEMORECEPTORS AND SYMPATHETIC RESETTING

Recent studies establish that the peripheral sympathetic activity may continue long after cessation of hypoxemia. Crabtree et al administered intermittent asphyxia to 5 healthy awake subjects over a 20 minutes period. Muscle sympathetic nerve activity increased throughout the period of asphyxia and remained elevated above control levels for upto 20 minutes after the release of stimulus. The authors hypothesized that carotid chemoreceptors are sensitized to hypoxia (74). This fits well with theories that sympathetic activity to adrenals or

peripheral vasculature promotes diurnal elevation of blood pressure, by remaining high long after the nocturnal episodic asphyxia stimulus is terminated. The final link is the activation of an endogenous organ vasoactive amine, such as vascular wall angiotensin, cleared from the arterial wall in response to repeated vasoconstriction - relaxation, which may lead acutely to vasoconstriction and chronically to smooth muscle hypertrophy and a more permanent form of hypertension (75).

4.3.4.5 THE ROLE OF AGE AND GENETICS

Age also plays a role in the pathogenic effect of hypoxia on the cardiovascular system. This is suggested by animal experiments (76). Hypothetically younger humans may develop less blood pressure elevation in response to chronic episodic asphyxia than older individuals. Middle aged and older individuals might then be more susceptible to develop hypertension with sleep apnea and less likely to revert to normal blood pressure after elimination of apnea.

4.3.4.6 EFFECT OF NON SPECIFIC STRESS

Behavioural stress in many forms has been shown to induce acute cardiovascular responses. Chronic stress and increased sympathetic nerve activity may contribute to primary hypertension. Thus a more general response to stress, including disruption of sleep architecture and reduced sleep efficiency could promote elevated blood pressure in episodic hypoxia.

5. PULMONARY HYPERTENSION IN OBSTRUCTIVE SLEEP APNEA:

In 1998, the world health organization conference on Pulmonary arterial hypertension (PAH) (77) recognized sleep disordered breathing as a secondary cause of PAH, PAH may be defined as an elevation in the mean pulmonary arterial pressure to atleast 20 mmHg at rest or 30 mmHg during exertion. PAH is usually mild although it could also be severe, resulting in cor pulmonale, a feature of pickwickian syndrome.

Since the study of Tilkian and colleagues (78) many studies have demonstrated that PAH is relatively common in patients with OSA (79)

Multiple mechanisms mediate nocturnal rise in pulmonary arterial pressure. These include alterations in blood gases, cardiac output lung volume etc. Diurnal PAH could be precapillary, capillary or postcapillary depending on the co-morbid conditions that may contribute to the development of PAH in OSA. Post capillary

PAH could be due to left ventricular hypertrophy and diastolic dysfunction caused by diurnal systemic hypertension. Loss of vascular surface area as may occur in COPD is an important cause of capillary PAH. Another important mechanism contributing to or mediating PAH in OSA is the presence of factors that cause constriction of pulmonary arterioles, typically due to hypoxia. The molecular mechanisms behind these are complex and multifactorial.

6. SLEEP APNEA AND GLUCOSE METABOLISM:

6.1 DIABETES AS A CAUSE OF SLEEP APNEA

Many studies have suggested that diabetic patients with autonomic neuropathy were more likely to manifest obstructive or central sleep apnea or both than those without autonomic neuropathy (80). Given that normal breathing during sleep is dependent on central respiratory motor control and upper airway patency, a major implication of the earlier reports is that central and OSA might be a consequence of autonomic dysfunction. More recently data from sleep heart health

study has provided compelling evidence for an independent relationship between sleep apnea and type 2 Diabetes (81) in a large cohort of community dwelling individuals without cardiovascular disease.

6.2 SLEEP APNEA AS A CAUSE OF DIABETES:

A growing body of evidence suggests that sleep apnea may independently contribute to the incidence of Type 2 Diabetes. Perhaps the best evidence for a causal link is found in two recent cohort studies that assessed the association of type 2 Diabetes (82). In the first study, habitual snoring in 2668 Swedish men was associated with a higher incidence of self reported diabetes over a 10 year period (82). The subsequent Nurses' health study (82) showed that the relative risk for Diabetes comparing snorers to non snorers was 2.03. Thus it remains to be seen whether sleep apnea mediates the observed association between snoring and the occurrence of type 2 diabetes Hypoxia and sleep fragmentation are the major mechanisms proposed to explain the association.

7. OSA AND LEFT VENTRICULAR SYSTOLIC/DIASTOLIC DYSFUNCTION

7.1 OSA AND SYSTOLIC HEART FAILURE

In humans, there are 2 kinds of studies relating left ventricular systolic dysfunction and OSA. First, studies in which patients with OSA have been assessed for the presence of left ventricular dysfunction(83-86) and second , studies assessing the prevalence of OSA in patients with established LV systolic dysfunction(87, 88). Both the studies have pointed to a significant correlation. Use of radionucleotide ventriculography is important because in obese subjects, using ECHO may be associated with technical difficulties.

The mechanisms by which OSA may impair LV systolic function are multiple. Hypoxia plays a critical role both by impairing myocardial contractility and through a host of other neurohumoral mechanisms.

7.2 OSA AND DIASTOLIC HEART FAILURE

Isolated LV diastolic failure with relative preservation of LV systolic function is the most common form of heart failure in elderly subjects. The pathophysiologic consequences of this form of heart failure relate to a hypertrophied non compliant LV.

Hemodynamic studies (89, 90) of patients with OSA have documented that pulmonary capillary pressure increases during the course of an obstructive apnea, indicating development of diastolic dysfunction. During obstructive apnea, LV

transmural wall thickness increases. This along with the hypoxemia may impair LV relaxation which impairs diastolic function (91). Repeated exposure to nocturnal hypertension and consequent development of OSA induced systemic hypertension and increased LV mass may also contribute to left ventricular diastolic dysfunction.

Although the prevalence of sleep apnea in patients with systolic heart failure has been systematically studied, the prevalence and the impact of OSA in diastolic heart failure need to be determined. In one study of (92) 20 patients with diastolic heart failure, approximately half of the patients had sleep apnea. It is speculated that OSA could be the cause of diastolic heart failure or the presence of OSA could contribute to the worsening of diastolic heart failure. In this regard, a preliminary study reports that the treatment of OSA improves diastolic dysfunction (84) which might be a significant finding.

8 ARRYTHMIAS IN OSA

Repetitive nocturnal apneas elicit severe derangements in cardiovascular homeostasis. Hypoxemia, hypercarbia, acidosis and adrenergic activation, increased afterload and rapid fluctuation in cardiac wall stress would reasonably contribute to tachycardia- bradycardia oscillations and atrial and ventricular

arrhythmias. A variety of AV arrhythmias including complete heart block and ventricular asystole during sleep have been observed in patients with OSA (93, 94, 95) and have been eliminated by either tracheostomy or by nasal CPAP.(93, 94)

Although the normal heart would be less likely to manifest malignant arrythmias, in the setting of severe obstructive apnea, the ischemic, hypertrophied or failing heart would be more succeptible (96). Nevertheles the activation of the diving reflex during apneas is very important in the genesis of arrhythmias.

Tachycardia- bradycardia oscillations

Patients undergoing Holter monitoring may be noted to have repetitive cyclic episodes of tachycardia and bradycardias during the night (97). These oscillations in cardiac rate are for the most part explained by changes in cardiac autonomic drive related to breathing pattern. During the apnea, incremental hypoxemia elicits the diving reflex so that bradycardia becomes progressively more marked. With termination of apneas, hyperapneas occurs with consequent activation of thoracic afferents which is vagolytic (98). Thus with resumption of

breathing, abrupt lung inflation interrupts vagal drive to the heart, resulting in rapid onset tachycardia.

Bradyarrythmias:

The primary response to hypoxia is bradycardia. Patients with OSA may be particularly succeptible to hypoxia induced bradycardia, because their peripheral chemoreflex is heightened, so that even during voluntary apneas, hypoxia elicits greater bradycardia than is seen in closely matched control subjects (99).Moreover patients with OSA who also have systemic hypertension or cardiac failure may have even more severe bradycardic response to obstructive apnea.

Ventricular arrhythmias:

There is a potential contribution of OSA to ventricular arrhythmias through ventricular ectopy during profound bradycardia as well as polymorphic ventricular tachycardia due to cardiac hypoxia/ischemia. They are more common in patients with CAD and are virtually eliminated with treatment. Atrial fibrillation has also been associated with OSA

MATERIALS AND METHODS

The study was conducted in the department of medicine and the department of physiology, Madras Medical College, during the period from August 2007 to August 2008.

Patients attending Madras medical college and government general hospital medical outpatient department were considered for the study.

STUDY DESIGN:

Cross – Sectional study to evaluate the occurrence of obstructive sleep apnea and hypopnea syndrome and its complications in obese individuals.

STUDY DURATION:

This study was conducted for a period of one year from August 2007 to August 2008.

INCLUSION CRITERIA:

1. Age 21 – 60 years
2. Body mass index (BMI) $\geq$30 Kg/m^2
3. Epworth sleepiness score $\geq$ 11

EXLUSION CRITERIA:

1. Those with insufficient sleep
2. Shift work
3. Psychiatric disturbances(depression)
4. Drugs (Both stimulants and sedatives)

5. Narcolepsy

A total of 60 patients were included in the study after fulfilling the criteria. Patients with BMI ≥ 30 Kg/m^2 were subjected to Epworth s sleepiness scoring and those with a score of ≥ 11 were considered for the study and a total of 60 patients were included in the study.

The subjects were interviewed in detail regarding the symptoms of sleep apnea namely snoring, fragmented sleep and excessive somnolence. Symptoms reported by the patients were confirmed by the relatives.

POLYSOMNOGRAPHIC RECORDING:

All the 60 individuals were subjected to an overnight 8 hour polysomnography (RMS). It included twelve channels, two for EEG in C4A1 and C3A2 positions.Two electroocculogram on either sides, surface chin electromyogram, electrocardiogram, pulse oximetry for arterial oxygen saturation, thermistor to detect nasal airflow, respiratory inductance plethysmography for

abdominal and chest wall movements, microphone for objective recording of snoring.

Polysomnographic recording was done from ten PM to six AM. All the subjects were asked to empty their bladder before the recording. Before application of electrodes, the skin was prepared with spirit. Sleep duration was defined as the total duration spent by the subjects in actual sleep that is exclusive of all the periods of awakenings in between.

Sleep stage scoring was done for each 30 second scoring epoch using standard criterion. The presences of respiratory events were noted. They were defined as

1. Apnea : periods of cessation of nasal airflow lasting for atleast ten seconds
2. Hypopnea : Reduction of airflow (70%) of baseline for greater than 10 seconds
3. Obstructive sleep apnea: periods of cessation of nasal airflow lasting for at least ten seconds, associated with continuing abdominal and chest wall movements.

And the main parameter used to quantify the respiratory event was

1. Apnea- Hypopnea index (AHI): The average number of apneas/ hypopneas for each hour of sleep.
2. AHI $\geq$ 5 was considered diagnostic of OSA.

For those individuals turning out to be positive for OSAHS a detailed search for the following complications were done

1. Systemic Hypertension: hypertension was defined as
    a) Known hypertensive on antihypertensive drugs
    b) A resting blood pressure greater than 140/90 mmHg on two separate occasions measured by an approximate sized cuff
2. Pulmonary Hypertension: A diagnosis of pulmonary hypertension was made when the pulmonary arterial pressure was more than 25 mmHg as by ECHO.
3. Coronary Arterial disease: ECG and/or ECHO evidence of coronary arterial disease in the form of ST/ T changes or Regional wall motion abnormalities in ECHO.
4. Ventricular dysfunction: Diastolic/ systolic dysfunction as measured by ECHO.
5. Increases Packed cell volume(PCV): PCV $\geq$ 50%

6. Diabetes Mellitus: Known diabetics on drugs or Fasting blood sugar >126 mg% and/or 2 hour post glucose tolerance test value >200mg%

OBSERVATIONS

BASELINE CHARACTERISTICS:

In this study 60 subjects participated (Obese individuals with an Epworth sleepiness score ≥ 11)

TABLE 1:

Among the individuals participated seven were in the 21-30 age group (11.66%) and twenty two were in the 31- 40 year age group (36.6%). Similarly eighteen individuals (30%) and thirteen individuals (21.66%) were in the 41-50 and 51-60 year age group respectively.

TABLE 2:

Fourty two individuals were males (70%) and eighteen were females (30%).

TABLE 3:

The mean BMI was 35.5 and majority of the subjects were in the BMI of 31-40 (fifty five subjects which comes to around 91.66%) and the rest were in the BMI above 40. (8.33%)

ANALYSIS OF SYMPTOMS:

TABLE 4:

Snoring was the major symptom analyzed and twenty five subjects who underwent the polysomnography had snoring. Of the twenty patients who were

diagnosed to have OSA as per polysomnography fifteen had snoring (66.6%) as told by them or their bed partners.

RESULTS FROM THE POLYSOMNOGRAPHIC STUDY:

TABLE 5:

The polysomnographic study showed that twenty out of sixty patients (33.3%) had OSA as defined by an AHI ≥ 5.

TABLE 5:

The distribution of AHI among the study population was

1. Forty subjects had AHI <5 (66.66%)
2. Thirteen subjects had AHI between five and fifteen (21%)
3. Seven subjects had AHI> fifteen (11.66%)

TABLE 6:

Among eighteen females who participated in the study ten had OSAHS (55.55%), and among the forty-two males who participated ten had OSAHS (23.80%).

TABLE 7:

Out of the twenty subjects who turned positive for OSAHS as per the polysomnography, none of them were in the 21 -30 year age group. Four out of the twenty two subjects (18.18%) in the 31-40 year age group had OSAHS. Similarly six of the eighteen individuals (33.33%) and ten of the thirteen individuals (76.92%) in the 41-50 year and 51-60 year age group had OSAHS respectively.

TABLE 8:

Of the twenty individuals who turned positive for OSAHS thirteen had mild and seven had severe OSAHS respectively.

TABLE 9:

Three out of the five individuals with BMI $\geq$ 40 who participated had OSAHS (60%) as opposed to seventeen of the fifty-five individuals with BMI between 31-40 (30.90%)

PREVALENCE OF VARIOUS COMPLICATIONS:

TABLE 10:

Of the twenty individuals who had OSAHS, eight (40%) had systemic hypertension as documented by a blood pressure > 140/90mmHg measured on two separate occasions with an appropriate sized cuff. One had isolated systolic hypertension, three had isolated diastolic hypertension and four had combined systolic and diastolic hypertension. (TABLE 11)

TABLE 12:

Three (15%) among the twenty subjects with OSAHS had Pulmonary arterial hypertension as documented by a pulmonary arterial pressure > 25 mmHg as per ECHO.

TABLE 13:

Five of the twenty patients had a Packed cell volume >50% (25%).

TABLE 14:

Six subjects (30%) with OSA had evidence of coronary artery disease as by ECG and/or ECHO.

TABLE 15:

Five (25%) of the twenty patients with OSAHS had evidence for systolic and/ or diastolic dysfunction as per ECHO.

TABLE 16:

Five subjects (25%) had diabetes mellitus out of the twenty who had OSAHS. Of them two are known diabetics who were already on drugs and three were diagnosed to have high blood sugars now.

TABLE 17:

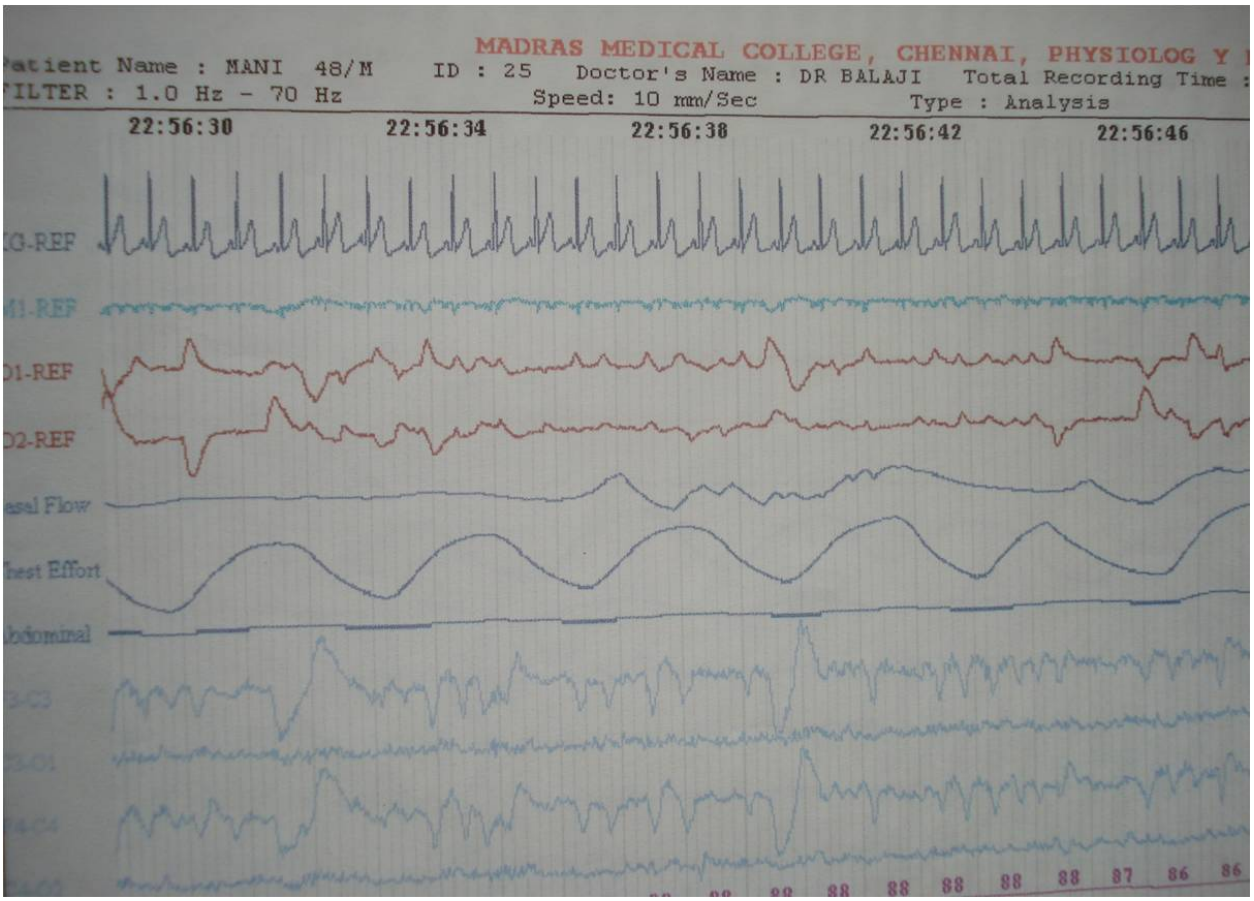
This table summarizes the prevalence of various complications associated with OSAHS.

Figure 2 shows the age and sex distribution of OSAHS among the individuals studied.

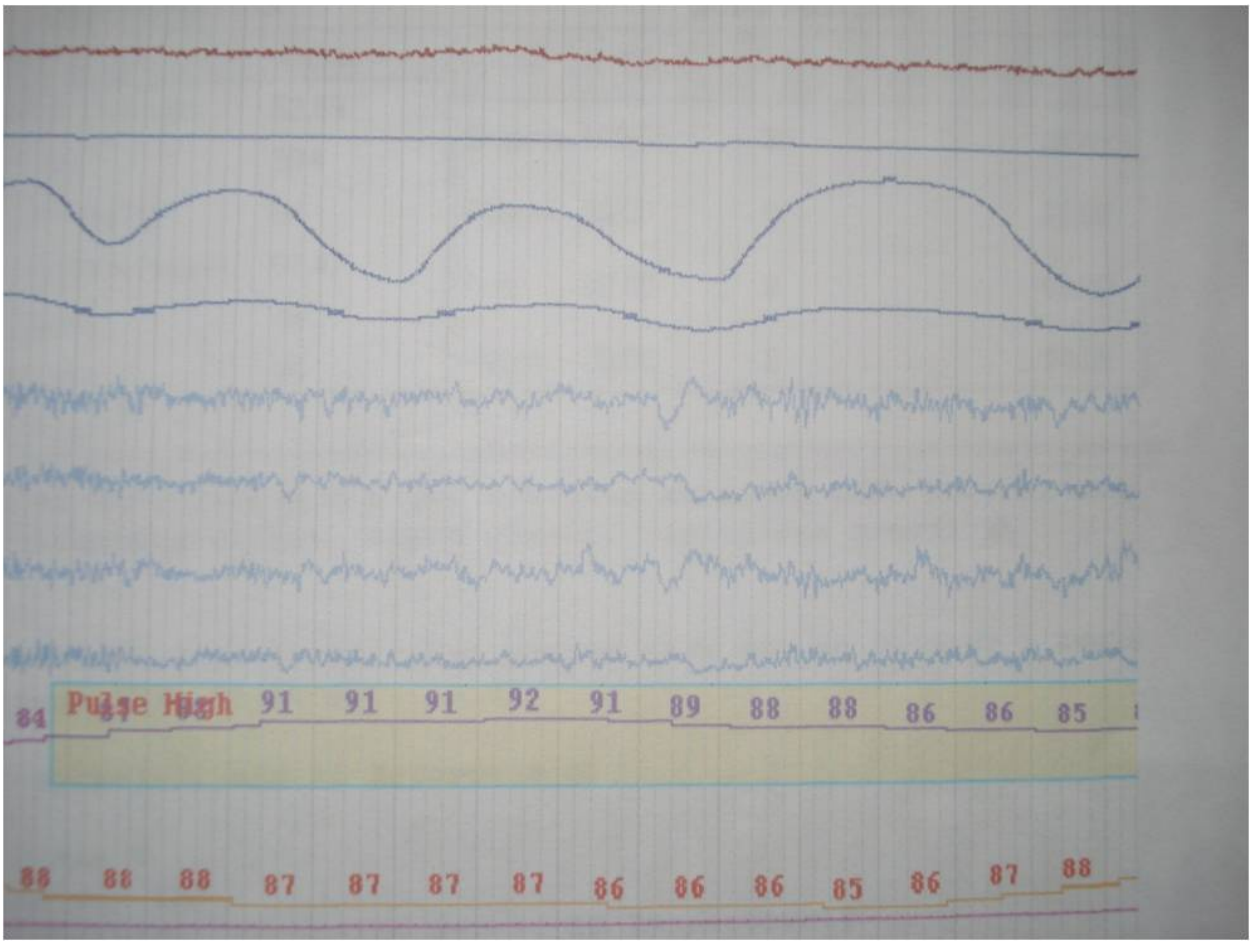
Figure 4 is a simple schematic diagram showing the relationship between OSAHS and the complications associated with it.

Figure 3 show the prevalence of cardiovascular risks over a seven year period in normal individuals as compared to ineffectively treated and completely treated OSAHS.

A Polysomnographic tracing showing the various parameters monitored



A Polysomnographic tracing showing an episode of Obstructive sleep Apnea



TABLES AND CHARTS

Age group	21-30	31-40	41-50	51-60
Number of individuals	7	22	18	13

Age distribution of individuals who participated in the study: Table 1

Sex distribution of individuals who participated in the study: Table 2

Sex	Male	Female	Total
Number of individuals	42	18	60

BMI of individuals who participated in the study: Table 3

BMI	30-40	>40
Number of individuals	55	5

Snoring and OSAHS: Table 4

	OSAHS (n=20)	Non-Apneics (n=40)
Snoring	15	10
No Snoring	5	30

In patients with BMI ≥30kg/m^2, snorers have a 9 times higher chance of having sleep apnea.

AHI of the subjects who participated in the study: Table 5

AHI	0-5	5-15	>15

Number of patients	40	13	7

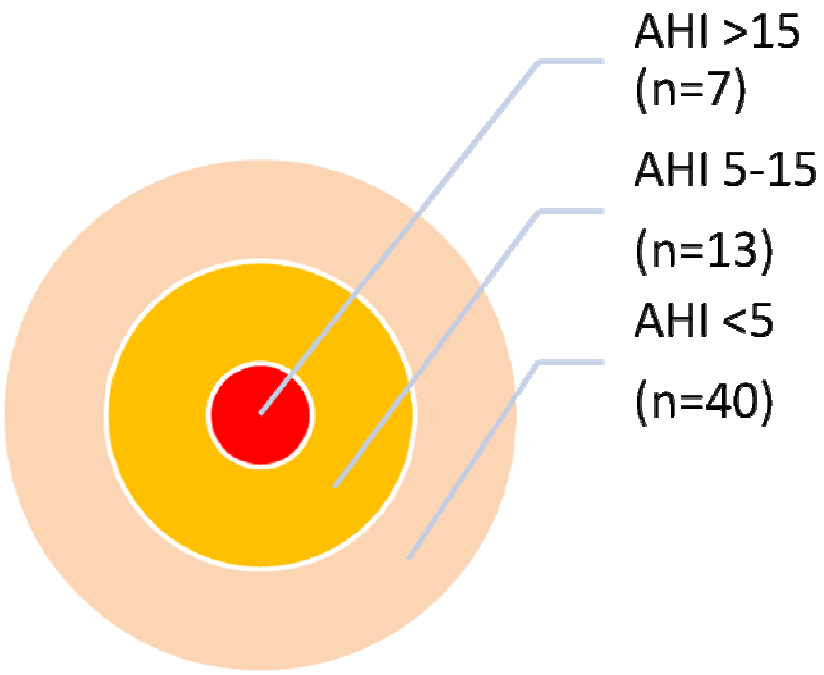


Figure 1:

Subjects who had OSAHS: Table x

	AHI <5	AHI>5
Number of subjects	40	20

Percentage of subjects who had OSAHS = 33.3%

Sex distribution of patients who turned positive for OSAHS: Table 6

	Males	Females	Total
Subjects participated	42	18	60
OSAHS	10	10	20
Percentage	23.80%	55.55%	33.33%

Age distribution of subjects who had OSAHS: Table 7

Age group	21-30	31-40	41-50	51-60
Subjects participated	7	22	18	13
OSAHS	-	4	6	10
Percentage	-	18.18%	33.33%	76.92%

Severity of OSA: Table 8

AHI	5-15(mild to moderate OSA)	>15 (severe OSA)
Number of subjects	13	7

BMI and OSAHS: Table 9

BMI	>40	30-40
Number of subjects participated	5	55
Positive for OSA	3	17
Negative for OSA	2	38

Blood pressure in patients with OSAHS: Table 10

Blood pressure	<140/90	>140/90
Number of subjects	12	8

Percentage of individuals with hypertension: 40%

Table 11:

Systolic hypertension	Diastolic hypertension	Combined hypertension
N=1	N=3	N=4

Pulmonary hypertension and OSAHS: Table 12

Pulmonary artery pressure	<20mmhg	>20mmhg
Number of subjects	17	3

Percentage of individuals with Pulmonary Hypertension: 15%

PCV and OSAHS: Table 13

PCV	<50%	>50%
Number of subjects	15	5

Percentage of individuals with PVC > 50%: 25%

CAD and OSAHS: Table 14

CAD(ECG and/or ECHO)	Yes	No
Number of subjects	6	14

Percentage of individuals with CAD: 30%

Systolic/Diastolic dysfunction and OSAHS: Table 15

Ventricular dysfunction	Yes	No
Number of subjects	5	15

Diabetes Mellitus and OASHS: Table 16:

Diabetes Mellitus	Yes	No
Number of subjects	5	15

Age and sex distribution of subjects with OSA

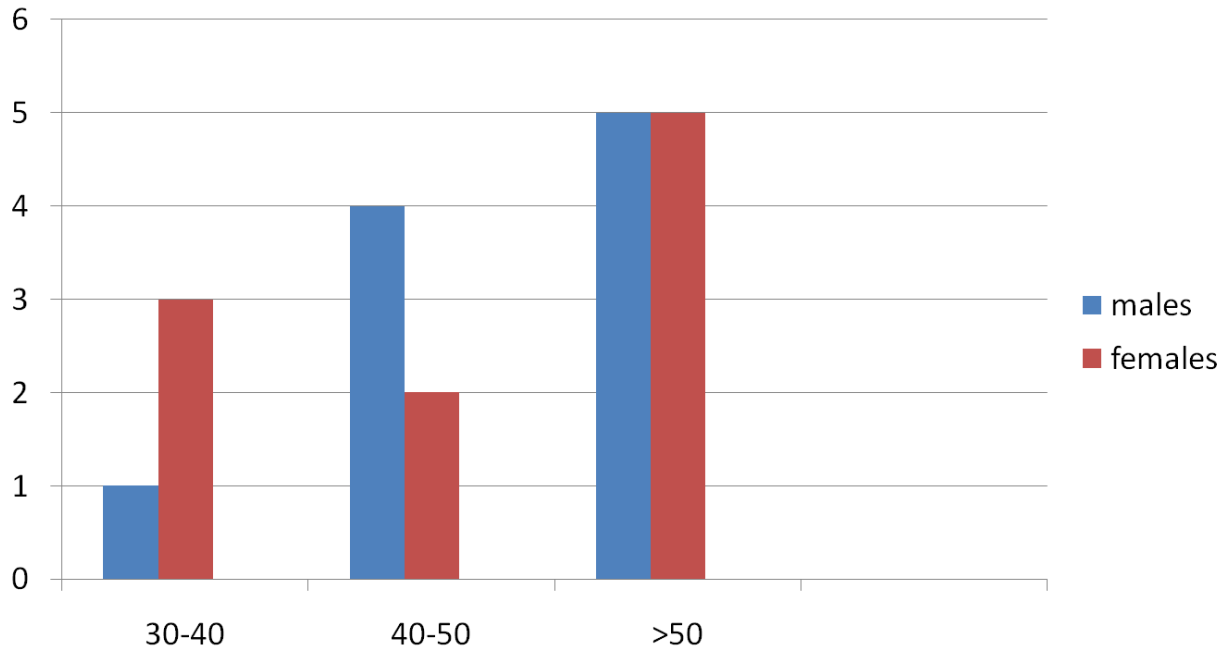


Figure 2:

Figure 3:

Incidence of cardiovascular risk – A 7 yr follow-up study

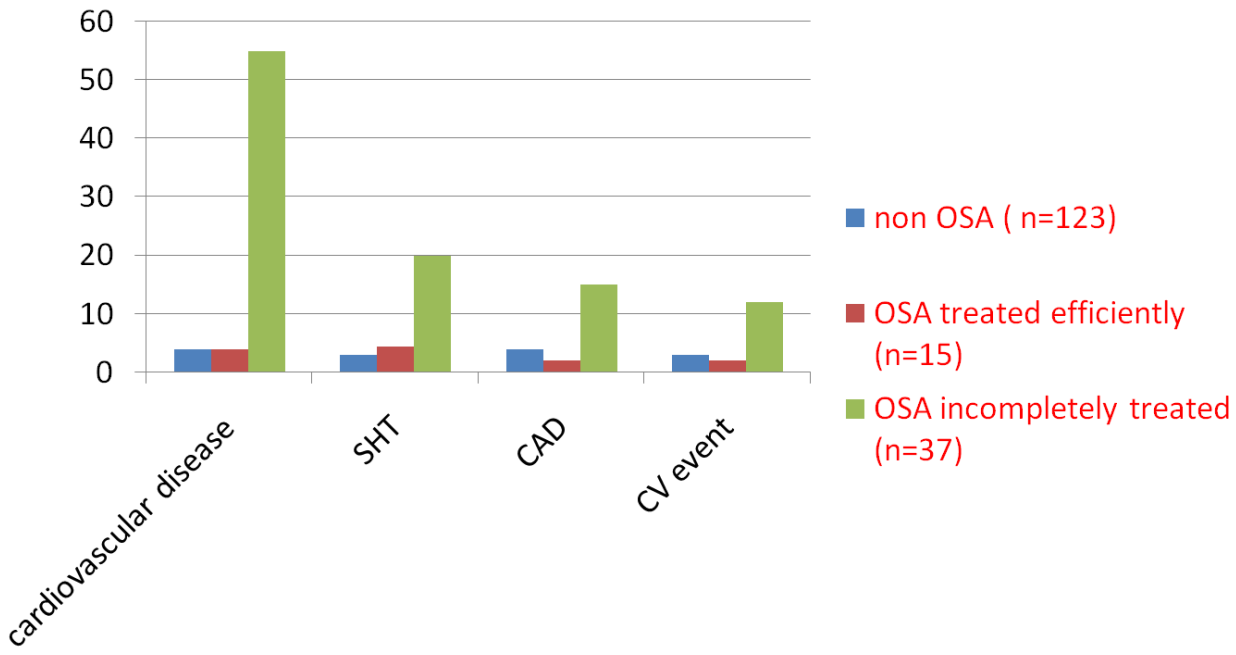


Figure 4:

Schematic of OSAHS and its complications

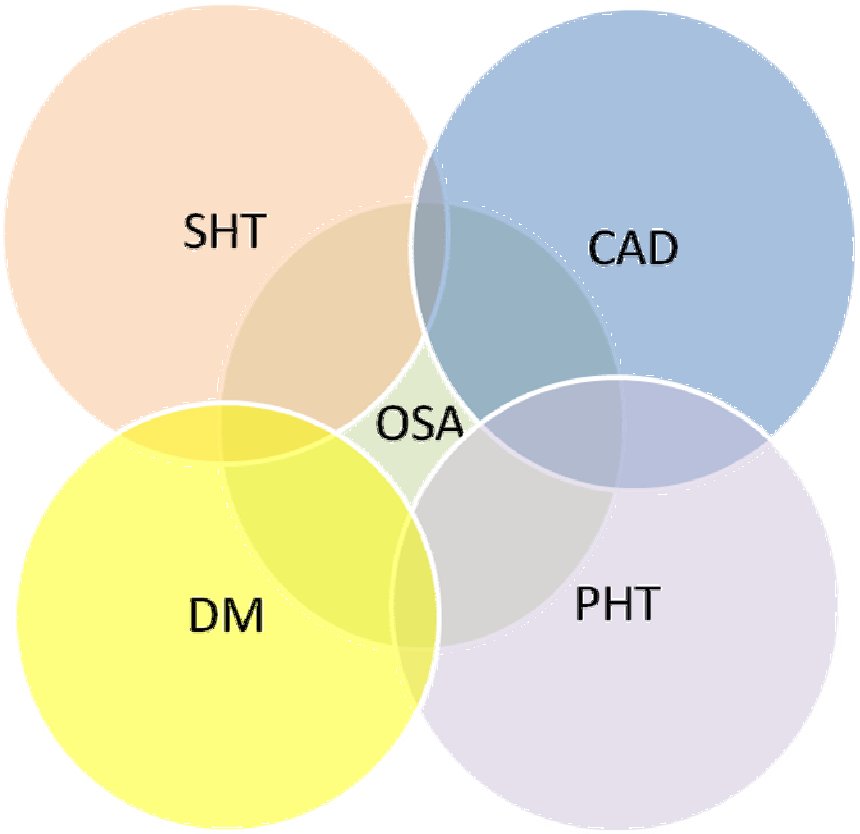


Table 17:

Prevalence of various complications of OSAHS

Complications	Percentage (%)
Systemic hypertension	40%
Pulmonary hypertension	15%
Coronary artery disease	30%
Ventricular dysfunction	25%
Diabetes Mellitus	25%
↑PCV	25%

DISCUSSION

Despite being an increasingly recognized entity in the western world, OSAHS is still not a commonly made diagnosis as far as our part of the country is concerned. As we could not get much literature on this as far as our population is concerned, we have planned to look out for the occurrence of OSAHS in obese individuals with excessive daytime somnolence as evidenced by an Epworth's sleepiness score ≥11.

The Prevalence of sleep apnea is reported to be approximately 30 %(23, 24 25) in the obese population and about 2.4%in the general population.

OSA is known to produce a multitude of complications starting from systemic hypertension to coronary artery disease and stroke etc. For example obesity predisposes to OSA and hypertension is also common due to various metabolic factors in obese subjects. There is increasing evidence that sleep apnea leads initially to nocturnal and later to daytime sustained hypertension.

We studied a group of obese individuals aged 21-60 years with an Epworth's score ≥ 11.

The occurrence of sleep apnea as per our study is 33.33% which is similar to many other studies in the western population (23, 24, 25). The prevalence is known

to increase with increasing age and age is supposed to be the most important predictor for the occurrence of OSAHS. We studied subjects in the age group from 21-60 and none of the subjects in the age group 21-30 had OSA as opposed to 76.92% of patients in the age group of 51-60 and 33.33% of subjects in the 41-50 year age group. In concordance with other studies age seems to be the single most important factor in the causation of OSAHS.

Ours is a male predominant study which contained 42 males and 18 females. The occurrence of OSA was higher in females as compared to the males (55.55% as against 27.80%). This is in contrast to other studies which generally report a higher prevalence in males as compared to females. The risk in women generally increases with obesity and postmenopausal state. This ratio may not be applicable to the UARS (Upper airway resistance syndrome) patients, where the ratio is close to 1:1.

Obesity also appears to be another important factor for OSAHS and the prevalence increases with increase in BMI. In our study too, the occurrence rate was around 60% in those with BMI > 40 as compared to 30.9% in those with a BMI between 30 – 40. In one study a BMI of atleast 25kg/m^2 had a sensitivity of 93% and a specificity of 74% for OSAHS (100). Thus it becomes important the diagnosis is thought of in individuals with a high BMI and with the symptoms.

Similarly excessive daytime sleepiness is an important symptom without which we will not be diagnosing OSAHS whatever may be the AHI. This was ascertained in our study by the Epworths sleepiness score (a score ≥11 was considered significant) (101).

Snoring seems to be another important symptom which can give us a clue regarding the presence of OSAHS though not all patients with snoring will have OSAHS. In our study snoring was present in 66% of the apneics as against 25% of the non-apneics and the odds ratio for individuals with snoring and OSAHS is 9 (Table 4).

OSAHS is associated with a number of complications many of which are correctable once treatmenr for OSAHS is started.

As many as half of the patients with sleep apnea may have underlying hypertension and many patients with hypertension, particularly resistant hypertension may have OSAHS. Infact there seems to be an interaction between OSA severity and resistance to Medications (102). Whether hypertension contributes to OSA remains unclear.

OSAHS patients maynot always have elevated systolic Blood pressure but may have high prevalence of isolated diastolic hypertension (103). One study suggested that there was a significant association between the incidence of

combined systolic and diastolic hypertension and the prevalence of sleep apnea in younger patients (< 60 years of age) but not in older patients (104). The prevalence of hypertension in our group was 40 %(n=80) (table 10) and most of the patients had combined systolic and diastolic hypertension (Table 11).

According to a study the four year incidence of hypertension was 31.5% as compared to 9.7% in OSAHS as compared to normals (105).

Various studies have documented an impressive reduction in systolic blood pressure with continuous positive airway pressure (CPAP) (106).

The prevalence of pulmonary hypertension is high in patients with OSAHS and it has been confirmed in many studies. An early study (107) in twelve patients with OSA who had undergone right heart catheterization showed cyclic changes in pulmonary artery pressure coinciding with episodes of OSA. Marked degree of hypoxemia and hypercapnia was associated with these hemodynamic abnormalities. In some of these patients the pulmonary arterial pressure exceeded 60mmhg. In some of these patients exercise increased the pulmonary capillary wedge pressure, unmasking left ventricular diastolic dysfunction. In our study the prevalence of pulmonary hypertension was 15% and was comparable to other studies which varies from 15-70% (108) and again CPAP treatment effectively

reduced the pulmonary artery pressure (109). Chaouat et al, Laks et al have done major works as far as the pulmonary hypertension and OSA is concerned.

Patients with OSAHS have a high prevalence of coronary artery disease and vice versa. The case control study of Perker et al (110) in a multiple logistic regression model showed that the presence of OSAHS remained independently associated with CAD (odds ratio 3.1 vs 9.8). The large Swedish cohort study of Moore et al (111) also suggests that OSA was much more prevalent in individuals with established CAD than in controls. Cross sectional reports from the population based sleep heart health study (112) showed that in patients with OSAHS the multivariable adjusted odds (95% limits) with self reported CAD was a more modest 1.27 (0.99 to 1.62) (comparing upper with lower quartiles of severity of sleep disordered breathing). The prevalence of OSA in our study was 30% which is in concordance with many other studies where the prevalence varies from 20-70 %(113).

Left ventricular dysfunction is more common in OSAHS (114) and OSA is also more common in patients with Left ventricular dysfunction (115). The prevalence ranges from 32 -50% (114) in different studies. Alchantis et al (116) studied 29 patients with severe OSA and 12 control subjects. The mean left ventricular ejection fraction was significantly lower in patients with OSA compared with the control group (52% versus 61%). After treatment with CPAP

the left ventriculat ejection fraction increased significantly to 56%. Left ventricular diastolic dysfunction also improved significantly. Jawaheri et al (117) found that 12 % of patients with Left ventricular ejection fraction < 45% have severe OSAHS. The sleep heart health study found that heart failure was 2.38 times more prevalent in mild to moderate OSA than in controls (112). The prevalence in our study group is 25% which is in accordance with the studies cited above.

Diabetes is more common in OSAHS and Diabetics are more prone to develop OSAHS. The occurrence of diabetes in our study group was 25%. Many studies have already found an undisputable correlation between OSAHS and Diabetes and the main evidence comes from two studies. In the first study, habitual snoring in 2668 Swedish men was associated with a higher incidence of self reported diabetes over a 10 year period. Obesity and habitual snoring were noted to be additive in their associated risks for type 2 diabetes. The major limitation of that study was that self-reports were used to asses diabetes and sleep apnea status. The pitfalls were subsequently addressed by data from the nurses' health study, in which the diagnosis of type 2 diabetes was made objectively. The relative risk for diabetes comparing regular snorers to non snorers was 2.03(95% confidence limits)

As far as the association between an increase in hematocrit and OSAHS is concerned further studies need to be done to support or to refute a causal association between the two. As of now there are quite a few studies which points to the hypoxia induced by OSAHS as a potential factor in the increased hematocrit cited. In our group 25% of the patients with OSAHS had a hematocrit more than 50% which goes very well in concordance with the works of J B Choi (118).

LIMITATIONS OF THIS STUDY

1. Since we have decided to just study the prevalence of various complications associated with OSAHS, we have not taken any controls. Had we taken controls, the association would have become even stronger.

2. Blood pressure was measured by ambulatory Blood pressure monitoring, measured the previous day and not on the night during polysomnography. This was done to avoid any sleep disturbance due to cuff inflation leading to arousal and hence affecting the polysomnographic data.

3. It would have been ideal to have monitored the BP using invasive techniques.This was not attempted for ethical reasons. However , since the ambulatory BP monitoring device could not be used while doing polysomnography recording, data regarding the stages of sleep viz a viz BP could not be obtained.

CONCLUSION

1. The occurrence of OSAHS in obese individuals with excessive daytime somnolence is 33.33%
2. The prevalence increases with age
3. Both the sexes are equally susceptible
4. Snoring is a common symptom and is present in 75% of individuals with OSAHS
5. Systemic hypertension, pulmonary hypertension, coronary artery disease, Left ventricular dysfunction, Diabetes and high PCV are all associated with OSAHS.
6. The prevalence of the above mentioned complications is comparable with other studies done so far.

SUMMARY

Obstructive sleep apnea syndrome is known to occur in about 30% of obese individuals and is also known to be associated with a number of complications. This study was undertaken as there are only limited data regarding the prevalence of this condition and the complications associated with it. A total of 60 obese individuals with excessive daytime somnolence as ascertained by an Epworth score greater than 11 were studied and a eight hour overnight polysomnographic recording was done and among the individuals who turned positive for OSAHS, various complications were assessed for their presence.

The occurrence of OSAHS was found to be about 33.33%. The prevalence of various complications were, systemic hypertension: 40%, Pulmonary hypertension: 15%, CAD: 30%, Ventricular dysfunction: 25%, Diabetes mellitus: 25%, elevated PCV: 25%.

BIBILIOGRAPHY:

1. Gastaut H, Tassinari CA, Duron B; Polysomnographic study of the episodic diurnal and nocturnal manifestations of the pickwickian syndrome, Brain Res 1965; 2 : 167 -186.

2. Bresnitz EA, Goldberg R, Epidemiology of obstructive sleep apnea, Epidemiol Rev 1994; 16: 210-217.

3. Olson LG, King MT, Hensley MJ, et al: A community study of snoring and sleep disordered breathing: Prevalence. Am J Respir Crit Care Med 1995; 152: 711-716.

4. Kripke DF, Ancoli- Israel S, Klauber MR, et al: Prevalence of sleep disordered breathing in ages 40-64: A population based survey. Sleep1997; 20:65-76.

5. Young T, Palta M, Dempsey J, et al: The occurrence of sleep disordered breathing among middle aged adults. N Engl J Med 1993; 328:1230-1235.

6. Ohayon MM, Guilleminault C, Priest RG, et al: Snonring and breathing pauses during sleep: Telephone interview survey of a United Kingdom population sample. BMJ 1997; 314:860-863.

7. Ip MS, Lam B, Laudwe IJ, et al: A community study of sleep disordered breathing in middle –aged Chinese men in Hong Kong. Chest 2001; 119:69-79.

8. Gislason T, Benedikisdottir B, Bjornsson JK, et al: Snoring, hypertension and sleep apnea syndrome. An epidemiologic survey of middle-aged women. Chest 1993; 103:1147-1151.

9. Guilleminault C: Obstructive sleep apnea: The clinical syndrome and historical perspective in. Thawley SE, Medical clinics of north America Vol 69 (6). WB Saunders company p 1157-1200, 1985.

10. Carskadon MA, Rechtschatten A, Monitoring and staging of human sleep apnea: Kruger MH, Roth T Principles and practice of sleep medicine. Philadelphia: W.B. Saunders; 65-682, 1989.

11. Snyder F, Hobson JA, Morrison DF and Goldfrank S: Changes in respiration, heart rate and systolic blood pressure in human slep, J Appl. Physiol. 19:417, 1964.

12. Richardson DW, Honour AJ and Goodman, AC, in Hypertension, ed. J.E. Wood III vol 16, P.62, New York, American heart association, 1968.

13. Smyth, H.S, Sleight, P, and pickering , G.W,: Regulation of arterial pressure during sleep in man. Clin. Res.24:109, 1989.

14. Brookes, H., and Carrol, J. H.: Clinical study of the effects of sleep and rest on blood pressure, Arch. Intern. Med.10: 97, 1912.

15. Littler, W.A: Sleep and blood pressure: Further observations, American Heart Journal.97: 35-37, 1979.

16. Irving J.B; Brash H.M, Kirby B.J: The value of ambulatory monitoring in borderline and established hypertension. Postgrad. Med.J. 194 52(suppl):137-139, 1976.

17. Shepherd, J.W: Cardiorespiratory changes in obstructive sleep apnea. In Kryger M.H., Roth, T., Dement, W.C.;eds, Principles and practice of sleep medicine, Philadelphia: W.B. Saunders: 537-551, 1989.

18. Brodsky, M., Wu, D., Deres, P., et al: Arrythmias documented by 24 hours continuous electrocardiographic monitoring in 50 male medical students without apparent heart disease. Am.J. Cardiology. 39:390-395, 1977.

19. Clarke, J.M., Shelton, J.R., Hamer, J., et al: The rhythm of normal heart. Lancet, 2, 508-512, 1976.

20. Camm, A.J., K.E., Ward, B.E., et al: The rhythm of normal heart in active elderly subjects. Am heart. J. 99: 598-603, 1986.

21. Flick, M.R.,and Block, A.J,: Nocturnal vs diurnal cardiac arrhythmias in patients with chronic obstructive lung disease. Chest, 75: 8-11, 1979.

22. Fleg. J.L.,Kennedy. H.L; Cardiac arrhythmias in healthy elderly population, Chest, 81:302-307, 1982.

23. Guilleminault, C., Van den Hoed, J., and Milier, M.M: Clinical overview,in, guilleminault. C., and Dement, W.C., (eds): Sleep apnea syndromes, New York. Alan. R.Liss. Inc.PP 1-12, 1988.

24. Boudolas, H., Schmidt. H.S., Clark, R.W., Geleris, P.,Scheal, S.F.,and Lewis, R.P;Anthropometric characteristics, cardiac abnormalitiesand adrenergic activity in patients with primary disorders of sleep. J.Med, 14:223-238,1983.

25. Desier, J.,Lavie, P., Onvat,A., and Chauzi,I:Sleep apnea syndromes in the morbidly obese as an indication for weight reduction. Annals of Surgery, 19:112-15, 1984.

26. Shepherd JW, Gefler W B, Guilleminault C, et al: Evaluation of the upper airway in patients with obstructive sleep apnea. Sleep, 14: 361-371, 1991.

27. Debery – Borowick B, Kukwa A, Blanks R H: Cephalometric analysis for diagnosis and treatment of obstructive sleep apnea. Laryngoscope, 98: 226-234, 1988.

28. Streizow, V V, Blanks R H, Basile A et al: Cephalometric airway analysis in obstructive sleep apnea syndrome. Laryngoscope, 88: 1149-158, 198.

29. Partinen M, Guilleminault C, Quera Salva MA et al: Obstructive sleep apnea and cephalometric roentgenogram: The role of anatomic upper airway abnormalities in the definition of abnormal breathing during sleep.Chest:93, 1199-1205, 1988.

30. Rivlin J., Hoffstein V, Kallofleisch J et al: Upper airway morphology in patients withidiopathic obstructive sleep apnea. Am Rev Respir Dis, 129:355-360, 1984.

31. Davies R J, Stradling J R: Neck circumference and other clinical features in the diagnosis of obstructive sleep apnea syndrome. Thorax: 101-105, 1992.

32. Schwab R J, Gefler W B, Hoffman E A, Gupta K B and pack A L: Dynamic upper airway imaging during awake respiration in normal subjects and patients with sleep disordered breathing. Am Rev Respir Dis, 148: 1385-1900, 1993.

33. Rajala R, Partinen M, Sane T , Pelkonan R, Huikuri K and Seppalainen A M: Obstructive sleep apnea syndrome in morbidly obese patients. J Int Med, 230: 125-129, 1991.

34. Millman R P, Caslille C C, Mcgarney S T et al: Body fat distribution and sleep apnea severity in women.

35. Camrgo C A: Obstructive sleep apnea and testosterone. Letter to the editor, N Engl J Med. 309: 314, 1983.

36. Strohl K P, Saunders N A, Scharf S M and Ingram: Progesterone administration and progressive sleep apnea. JAMA 245, 1230-1250, 1981.

37. Fisher J G, De la Pena A, Mayfield D and Flickinger R: Starvation and behavior modification as a treatment in obese patients with sleep apnea- a follow up. Sleep Res, 7: 222, 1978.

38. Harman EM, Wynni JW and Block AJ: The effect of weight loss on sleep disordered breathing and oxygen desaturation in m orbidly obese men. Chest, 82: 291-293, 1982.

39. Orr WC, Martin RJ, Imes NK, Rogers RM and Stahl MC: Hypersomnolent and nonhypersomnolentpatients with upper airway obstruction during sleep. Chest, 75:418-422, 1979.

40. Guilleminault C, Eldridge F C, Tilkian A, Simman FB and Dement W:Sleep apnea syndromes due to upper airway obstruction. Arch Intern Med, 137:296-300, 1977.

41. Marglus DL, Lewis M, Shibuya and Pert CB: Beta endorphin is associated with overeating in genetically obese mice or rats. Science, 202: 988-991, 1975.

42. McCloy J and McCloy RF: Encephalins, hunger and obesity.Lancet, 2: 156, 1979.

43. Moss IR, Friedman E: Beta-endorphin: Effects on respiratory regulation. Life Sci, 23: 1271-1276, 1978.

44. Tilkian AG, Guilleminault C,Schorderer JS et al: Hemodynamics in sleep induced apnea: studies during wakefulness and sleep. Annals of Internal Medicine, 85: 714-719, 1976.

45. Stradling JR, Crosby JH: Relationbetween systemic Hypertension and sleep hypoxemia or snoring: Analysis of 748 men drawn from general practice. BMJ,300:75-78,1990.

46. Lavie P, Ben Yousuf R, Rubin AE: Prevalence of sleep apnea syndrome among patients with essential hypertension. Am Heart J, 108:373-376, 1984.

47. Kates A, Cardieux RJ, Shaw LC et al .Sleep apnea in a hypertensive population. Lancet,ii: 1005-1008,1984.

48. Williams AJ, Houston D,Finberg S et al: Sleep apnea syndromes and essential hypertension. Am J Cardiol. 55:1019-1022,1985.

49. Mateika JH, Mateika S, Slutsky AS, Hoffstein V: The effect of snoring on mean arterial blood pressure during NREM sleep. Am Rev Respir. Dis. 145:141-146, 1992.

50. Guilleminault C, Simmons FB, Motta J et al: Obstructive sleep apnea syndrome and tracheostomy. Arch. Intern Med. 141:987-988, 1981.

51. Guilleminault C, Suzuki M: Sleep related hemodynamics and hypertension with partial or complete upper airway obstruction during sleep. Sleep, 15(65)520-524, 1992.

52. Mayer J, Becker H, Bandenburg et al: Blood pressure and sleep apnea, results of long term nasal continuous positive airway pressure therapy. Cardiology, 2: 847-852, 1989.

53. Fletcher EC,DeBenhke RD, Lovol MS, Gorin AB: Undiagnosed sleep apnea in patients with essential hypertension. Ann Int Med, 103: 190-195, 1985.

54. Wilcox I, Grunstein RR, Hedner J A et al: Effect of nasal continuous positive airway pressure in obstructive sleep apnea. Sleep 16: 539-544, 1993.

55. Hirshkowitz M, Karacan I, Gurakar H, William R L: Hypertension, erectile dysfunction and occult sleep apnea.Sleep, 12: 223-232,1989.

56. Warley A R H, Mitchell A H, Stradley J R: Prevalence of nocturnal hypoxemia in men with and without hypertension. Q J Med 68: 637-644, 1988.

57. Hoffstein V: Blood pressure, snoring obesity and nocturnal hypoxemia. Lancet, 344 643-645,1994.

58. Hla K M, Young T B, Bidwell T et al: Sleep apnea and hypertension – a population based study. Ann Int Med, 120:382-388, 1994.

59. Somers V, Javala D C, Mark A L and Abboud F M: Sympathetic nerve response to hypoxia during breathing and apnea in normal humans. Circulation, 76(supp 4) 48, 1987.

60. Somers V, Mark A L, Abboud F M: Interaction of baroreceptor and chemoreceptor reflex control of sympathetic nerve activity in normal Humans. J. Clin. Invest, 87: 1953-1957, 1991.

61. Fletcher E C, Miller J Schawb JW, Fletcher J G: Urinary catecholamines before and after tracheostomy in obstructive sleep apnea and hypertension. Sleep, 10: 35-44, 1987.

62. Blumberg H, Oberle J: Effect of systemic hypoxia and hypercapnia on skin and muscle sympathetic activity in humans. Pfugers Arch, 403(s):R51, 1985.

63. Shepherd J W: Gas exchange during sleep. Medical clinics of North America, 69(6): 1243-1264, 1985.

64. Van den Aardwerg J, Karemaker JM: Repetitive apneas induce periodic hypertension in normal subjects through hypoxia. J Appl Physiol, 72(3): 821-827, 1992.

65. Lavie P, Yoff N, Berger I: The relationship between the severity of the sleep apnea syndrome and 24 hours blood pressure value in patients with obstructive sleep apnea. Chest, 103: 717-721, 1993.

66. Hednef JA, Wilcox I, Lakso T et al: A specific and pressor effect of hypoxia in patients with sleep apnea. Am Rev Respir Dis, 146: 1240-1245, 1992.

67. Shimuzu T, Kogawa S, Tashiro T et al: Transient elevation of blood pressure in obstructive apnea, in Honnej,ed. Sleep 90- Biochem West Germany : Pontager 1990: 182-184.

68. Ringer J, Basner R C, Shannon R et al: Hypoxemia alone doesnot explain blood pressure elevation after obstructive apneas. J Appl Physiol, 69(6): 2143-2148,1990.

69. Hedner J, Ejnell H, Sellgren J et al: High muscle sympathetic nerve activity in sleep apnea syndrome. J Hypertens, 6: s529-s531,1988.

70. Fletcher E C, Miller H: Urinary catecholamines before and after tracheostomy in obstructive sleep apnea and hypertension. Sleep, 10: 35-44,1987.

71. Marrone O, Riccobona L, Salvagguo A et al: Catecholamines and blood pressure in obstructive sleep apnea syndrome. Chest 103, 722-727,1993.

72. Somers V K, Mark A C, Zavala D C: Influence of ventilation and hypocapnia on sympathetic response to hypoxia. J Appl Physiol, 67: 2095-2100,1989.

73. Guyton A, Arterial pressure regulation. In Prebelbis D ed, Textbook of medical physiology. Philadelphia. WB Saunders, 244-256,1986.

74. Crabtree D, Morgan B, Skatrud J: Chemoreceptor sensitization augments sympathetic vasomotor outflow in awake humans. Am Rev. Respir Dis, 147: A 1015(Abstr), 1993.

75. Dzau V J, Gibbons G H, Pralt R E: Molecular Mechanisms of vascular rennin angiotensinogen system in myointimal hyperplasia. Hypertension 18 (Suppl 11) 11100-11105,1991.

76. Clerour JC, Granattasio C, Bolle G et al: Deceased cardiopulmonary reflexes with aging in normotensive humans- Am J Pjysiol, 1790-1799, 1989.

77. Rich S (ed): Primary pulmonary Hypertension: Executive summary from the world symposium on Primary pulmonary hypertension. Geneva, WHO, 1998.

78. Tilkian AG, Guilleminault C et al: Hemodynamics in sleep induced apnea. Studies during wakefulness and sleep. Ann Intern Med 1976; 85: 714-719.

79. Marrone O, Bonsignore MR: Pulmoary hemodynamics in obstructive sleep apnea. Sleep Med Rev 2002;6: 175-193

80. Ficker JH, Dertinger SH, Siegfried W, et al: Obstructive sleep apnea and diabetes mellitus: The role of cardiovascular autonomic neuropathy. Eur Respir J 1998; 11:14-19.

81. Resnick HE, Redline S, Shahar E, et al: Diabetes and sleep disturbances: Findings from the sleep heart health study. Diabetes Care 2003; 26:702-709.

82. Elmasry A, Janson C, Lindboy E, et al: The role of habitual snoring and obesity in the development of diabetes: A 10 year follow-up study in a male population. J. Intern Med 2000; 248: 13-20.

83. Hanly P, sasson Z, Zuberi N et al: Ventricular function in snorrs and patients with obstructive sleep apnea. Chest 1992; 102: 100-105.

84. Alchanatis M, Tourkohoriti G, Kosmas EN et al: Evidence of left ventricular dysfunction in patients with obstructive sleep apnea. Eur Respir J 2002; 20: 1239-1245.

85. Laaban JP, Fascal Sebaoun S, Bloch E et al: Left ventricular dysfunction in patients with obstructive sleep apnea syndrome. Chest 2002; 22: 1133-1138.

86. Shahar E, Whitney CW, Redline S et al: Sleep –disordered breathing and cardiovascular disease: cross sectional results of the sleep heart heath study. Am J Respir Crit Med 2001; 163: 19-25.

87. Javaheri S, Parker TJ, Liming JD et al: Sleep apnea in 81 ambulatory male patients in stable heart failure: Types and their prevalences , consequences and presentations. Circulation 1998; 97:2154-2159.

88. Sin DD, Fitzgerald F, Parker JD, et al: Risk factors for central and obstructive sleep apnea in 450 men and women with congestive heart failure. Am J Respir Crit Care Med 1999; 160:1101.

89. Tilkian AG, Guilleminault C, Schroderer JS et al: Hemodynamics in sleep – induced apnea : Studies during wakefulness and sleep. Ann Intern Med 1976;85:714-719.

90. Buda AJ, Schroderer JC, Guilleminault C: Abnormalities of pulmonary artery wedge pressure in sleep – induced apnea. J Cardiol 1981; 1: 67-74.

91. Cargill JI, Kelly DG, Liworth BJ: Adverse effects of hypoxemia on diastolic filling in humans. Clin Sci 1995; 89:165.

92. Chan J, Sanderson J, Chan W et al: Prevalence of sleep disordered breathing in diastolic heart failure. Chest 1997; 111: 1488-1493.

93. Guilleminault C, Connolly SJ, Winkle RA: Cardiac arrhythmia and conduction disturbances during sleep in 400 patients with sleep apnea syndrome. Am J Cardiol 1983; 52:490-494.

94. Koehler E, Fus E, Grimm W et al: Heart block in patients with obstructive sleep apnea: Pathogenetic factors and effects of treatment. Eur Respir J 1998;11:434-439.

95. Grimm W, Hoffmann J, Menz V et al: Electrophysiological evaluation of sinus node function and atrioventricular conduction in patients with prolonged ventricular asystole during obstructive sleep apnea. Am J Cardiol 1996; 77:1310-1314.

96. Koehlar U, Glaremin DT, Junkermann H, et al: Nocturnal myocardial ischemia and cardiac arrhythmia in patients wih sleep apnea with and without coronary artery disease. Klin Wochenchr 1991; 69:474-482.

97. Roche F, Gaspoz JM, Court-Fortune I, et al: Screening of obstructive sleep apnea syndrome by heart rate variability analysis. Circulation 1999;100:1411-1415.

98. Anrep GV, Pascual W, Rossler R: Respiratory variations of the heart rate: II. The central mechanism of the respiratory arrhythmia and the interrelations between the central and reflex mechanisms. Proc R Soc Lond Ser B 1936;119:218-230.

99. Narkiewicz K, Van de borne P, Pesek C, et al: Selective potentiation of peripheral chemoreceptor sensitivity in obstructive sleep apnea. Circulation 1999;99:1183-1189.

100. Grunstein R, Wilcox I, Yang T et al: Snoring and sleep apnea in men: Association with central obesity and hypertension. Int J Obes;17: 533-540.

101. Harrison's principles of internal medicine 17th Ed: Chapter 259: Sleep apnea, P.No 1666. Table 259-2.

102. Lavie P, Hoffstein V, Sleep apnea syndrome: A possibly contributing factor to resistant hypertension. Sleep 2001;24:721-725.

103. Sharahi Y, Scope A, Dagan Y, Diastolic pressure is the first to rise in association with easy subclinical obstructive sleep apnea. Lessons from periodic examination screening. Am J Hypertens 2003;16:236-239.

104. Hass DC, Foster GL, Nieto FJ, Redline S: Age dependent associations between sleep disordered breathing and hypertension. Circulation 2005; 111:614-621.

105. Peppard PE, Young T: Prospective study of the association between sleep disordered breathing and hypertension. N Engl J Med 2000;342: 1378-1384.

106. Pepperell JC, Ramdassingh D, Crosthwaite N, et al: Ambulatory blood pressure after therapeutic and subtherapeutic nasal continuous positive airway pressure for obstructive sleep apnea. A randomized parallel tral. Lancet 2002;359:204-210.

107. Tilkian HG, Guilleminault C, Schroeder JS, et al: Hemodynamics in sleep induced apnea. Studies during wakefulness and sleep. Ann Intern Med 1976;85:714-719.

108. Bady E, Echkar A, Pascal, et al: Pulmonary arterial hypertension in patients with sleep apnea syndrome. Thorax 2000;55:934-939.

109. Sforza E, Krieger J, et al: Long term effects of treatment with nasal continuous positive airway pressure on daytime lung function and pulmonary hemodynamics in patients with obstructive sleep apnea. Am Rev Respir Dis 1990;141:866-870.

110. Peker Y, Kraiczi H, Hedner J, et al. An independent association between obstructive sleep apnea and coronary arterial disease. Eur Respir J 1999;14:179-184.

111. Mooe T, Rabben T, Wiklund U et al. Sleep disordered breathing in men with coronary arterial disease. Chest 1996;109:659-663.

112. Shahar E, Whitney CW, Redline S et al: Sleep disordered breathing and cardiovascular disease.Cross sectional reports of the sleep heary health study. Am J Resir Crit Care Med 2001; 163: 19-25.

113. Akasaka K, Akiba Y, et al : Association between sleep apnea syndrome and coronary artery disease Nippon Kyobu Shikash Gakkai Zashi: 1997;35:16-21.

114. Hansy P, Sasson Z et al: Ventricular function in snorers and patients with obstructive sleep apnea. Chest 1992; 102:100-105.

115. Javaheri S, Pankar TJ, et al: Slep apnea in ambulatory patients with stable heart failure. Circulation 1998;97:2154-2159.

116. Alchanatis M, Tourkohoriti G, Kosmas EN, et al: Evidence of left ventricular dysfunction in patients with obstructive sleep apnea syndrome. Eur Respir J 2002;20:11239-1245.

117. Javaheri S, Sleep disorders in systolic heart failure:A prospective study of 100 male patients. The first report. Int J Cardiol 2006;106:21-28.

118. J.B. Choi, PJ Mills, Sleep breat 2006;10:155-160.

LIST OF TABLES

LIST OF FIGURES

ABBREVIATIONS

OSAHS - Obstructive sleep apnea- Hypopnea syndrome

UARS - Upper airway resistance syndrome

REM - Rapid eye movement

EEG - Electroencephalogram

EOG - Electroocculogram

EMG - Electromyogram

BP - Blood Pressure

AHI - Apnea Hypopnea Index

BMI - Body mass Index

CPAP - Continuous Positive airway pressure

PAH - Pulmonary arterial hypertension

LV - Left Ventricle

CAD - Coronary Arterial Disease

DM - Diabetes Mellitus

SHT - Systemic Hypertension

FBS - Fasting blood sugar

PPBS - Post Prandial blood sugar

PROFORMA

OCCURRENCE OF OBSTRUCTIVE SLEEP APNEA/HYPOPNEA SYNDROME AND ITS COMPLICATIONS IN OBESE INDIVIDUALS

NAME:

AGE:

SEX:

BMI:

EPWORTH'S SLEEPINESS SCORE:

HISTORY: 1) History of snoring (self reported or by bed partner)

2) History of polyuria (more than one awakening in night for micturition)

EXAMINATION:

Detailed general examination including

a) Height, weight and BMI

b) Neck circumference

c) Anaemia, cyanosis, pedal edema.

Cardiac examination in detail:

a) Pulse

b) Blood Pressure

c) Jugular venous pressure

d) S1 ,S2 , P2

e) Added sounds

Respiratory examination in detail:

a) Examination of thoracic cage for any deformity

b) Tracheal position

c) Breath sounds

d) Added sounds

POLYSOMNOGRAPHY:

AHI:

Analysis of complications in those with OSAHS:

1) Blood pressure (measured twice on two different occasions 24 hours apart)

2) Electrocardiogram

3) Echocardiogram

4) Pulmonary arterial pressure measured by ECHO

5) Packed cell volume

6) Blood sugar (Fasting and 2 hour post Glucose tolerance test)

EPWORTH'S SLEEPINESS SCORE:

0 = would never dose

1 = Slight chance of dosing

2 = Moderate chance of dosing

3 = High chance of dosing

a) Sitting and reading

b) Watching TV

c) Sitting inactive in a public place (eg: in a theatre or at a meeting)

d) As a passenger in a car for one hour without break

e) Lying down to rest in the afternoon

f) Sitting and talking to someone

g) Sitting quietly after lunch without alcohol

h) In a car, while stopping for a few minutes in traffic

Total score:

Patient consent form

Study Title:

"Occurrence of Obstructive sleep apnea and its complications in obese individuals"

Study centre : Institute of Internal Medicine ,Madras Medical College.

Patient's Name :

Patient's Age :

Identification Number:

Patients may check ( ) these Boxes

I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask the questions and all my questions and doubts have been answered to my complete satisfaction.
[ ]

I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving any reason , without my legal rights being affected.
[ ]

I understand that the sponsor of the clinical study, others working on the sponsor's behalf, the ethics committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from study. I agree to this access. However, I understand that my identitiy would not be revealed, in any information released to third parties or published,unless as required under the law. I agree not to restrict the use of any data or results that arise from this study.

[ ]

I agree to take part in the above study and to comply with the instructions given during the study and to faithfully to co-operate with the study team, and to immediately inform the study staff if I suffer from any deterioration in my health or my wellbeing or any unexpected or unusual symptoms.
[ ]

I hereby give consent to participate in this study looking for the prevalence of obstructive sleep apnea and its complications in obese individuals. I have understood that as a part of this study I

will be required to sleep for eight hours in the night with various medical equipments attached.
[ ]

Signature /Thumb impression

Of the patient : Place:

Patient's name and address: …….

Signature of the investigatior: ……. Place…….
Date…….

MASTER CHART

AHI of Individuals who participated in the study

S.No	Age	Sex	Epworth score	AHI	Sleep duration	Snoring	BMI
1	48	M	13	4	6	N	35
2	25	M	14	2	6	N	38
3	58	F	12	3	7	N	32
4	52	M	14	17	8	y	38
5	42	M	15	3	7	N	33
6	55	M	12	18	8	y	34
7	57	M	14	16	7	y	38
8	42	F	13	4	8	N	36
9	50	F	12	14	8	y	35
10	39	F	11	16	8	y	33
11	30	M	12	4	6	N	32
12	30	M	11	3	7	y	32
13	33	M	12	2	8	y	33
14	54	M	13	13	8	y	33
15	60	M	13	15	8	y	35
16	36	F	13	3	8	N	33
17	45	M	12	3	7	N	36
18	40	M	12	4	7	N	32
19	30	M	12	2	6	y	33
20	50	M	13	16	8	y	34
21	58	F	14	12	8	y	35
22	53	F	14	8	6	y	35
23	28	M	14	1	7	N	31
24	38	M	17	3	8	y	31

25	35	M	16	2	8	N	32
26	42	M	16	13	8	y	32
27	35	M	12	3	8	y	33
28	40	M	12	2	8	N	38
29	29	M	11	4	8	N	41
30	30	M	12	4	7	N	32
31	48	M	13	4	7	N	31
32	40	M	13	2	6	N	33

.

AHI of Individuals who participated in the study

S.No	Age	Sex	Epworth score	AHI	Sleep duration	Snoring	BMI
33	46	M	14	2	8	N	33
34	58	F	14	11	7	y	33
35	57	M	11	3	8	y	36
36	50	F	12	3	8	N	32
37	55	M	12	4	8	N	31
38	44	M	12	7	8	y	32
39	45	M	13	12	8	y	35
40	36	F	13	4	8	y	33
41	37	M	12	3	8	N	35
42	36	M	11	1	7	y	33
43	37	M	14	7	8	y	38
44	45	M	12	3	7	N	34
45	40	M	12	2	6	N	33
46	55	F	14	8	8	y	35
47	45	M	12	3	6	y	35
48	38	M	12	1	7	y	32
49	38	F	12	2	8	N	38
50	40	F	17	18	8	y	49
51	35	F	12	1	8	N	40
52	39	F	12	11	8	y	42
53	56	F	13	8	7	y	37

54	50	F	13	2	8	N	35
55	40	M	16	2	8	N	31
56	45	M	14	12	8	y	40
57	40	M	12	2	7	N	35
58	36	M	12	1	7	N	33
59	44	M	12	4	7	N	36
60	50	M	13	3	8	N	32

AHI of Individuals who turned positive for OSAHS

S.No	Age	Sex	BMI	AHI	Sleep duration
1	52	M	38	17	8
2	55	M	34	18	8
3	57	M	38	16	8
4	50	M	35	14	7
5	39	M	33	16	8
6	54	M	33	13	7
7	60	M	35	15	8
8	40	F	49	18	6
9	39	F	42	11	8
10	50	M	34	16	7
11	58	F	35	12	8
12	53	M	35	8	8
13	42	M	32	13	8
14	56	M	37	8	7
15	45	M	40	12	7
16	58	F	33	11	7
17	44	F	32	7	7
18	45	M	35	12	8
19	37	M	38	7	8
20	55	F	35	8	7

Prevalence of various complications in individuals with OSAHS

S.No	Age	Sex	BMI	AHI	Sleep duration	BP	PCV	CAD	LV dysfunction	PAP	FBS	PPB
1	52	M	38	17	8	150/100	37	N	Y	30	110	130
2	55	M	34	18	8	140/100	52	Y	N	17	90	150
3	57	M	38	16	8	130/100	45	Y	Y	12	80	140
4	50	M	35	14	7	126/86	38	N	N	18	75	138
5	39	M	33	16	8	134/84	50	Y	Y	17	85	128
6	54	M	33	13	7	146/96	42	N	N	16	95	138
7	60	M	35	15	8	120/80	48	N	N	15	100	130
8	40	F	49	18	6	126/86	52	N	N	12	104	140
9	39	F	42	11	8	130/80	38	N	N	13	140	220
10	50	M	34	16	7	158/88	54	Y	N	14	90	160
11	58	F	35	12	8	150/104	34	N	N	15	120	260
12	53	M	35	8	8	148/100	32	N	N	15	80	160
13	42	M	32	13	8	110/84	45	N	N	16	130	250
14	56	M	37	8	7	136/88	51	N	N	13	90	150
15	45	M	40	12	7	126/80	38	N	Y	28	75	140
16	58	F	33	11	7	120/86	45	Y	N	15	135	225
17	44	F	32	7	7	110/70	39	N	N	12	80	140
18	45	M	35	12	8	130/100	45	Y	Y	34	80	138
19	37	M	38	7	8	130/86	42	N	N	15	120	210
20	55	F	35	8	7	120/86	42	N	N	18	90	130